Increased Activity in Human Visual Cortex during Directed Attention in the Absence of Visual Stimulation

Sabine Kastner,*‡ Mark A. Pinsk,* Peter De Weerd,*
Robert Desimone,† and Leslie G. Ungerleider*
*Laboratory of Brain and Cognition
†Laboratory of Neuropsychology
National Institute of Mental Health
National Institutes of Health
Bethesda, Maryland 20892

Summary

When subjects direct attention to a particular location in a visual scene, responses in the visual cortex to stimuli presented at that location are enhanced, and the suppressive influences of nearby distractors are reduced. What is the top-down signal that modulates the response to an attended versus an unattended stimulus? Here, we demonstrate increased activity related to attention in the absence of visual stimulation in extrastriate cortex when subjects covertly directed attention to a peripheral location expecting the onset of visual stimuli. Frontal and parietal areas showed a stronger signal increase during this expectation than did visual areas. The increased activity in visual cortex in the absence of visual stimulation may reflect a top-down bias of neural signals in favor of the attended location, which derives from a fronto-parietal network.

Introduction

Visual scenes contain typically many different objects, which cannot all be processed simultaneously due to the limited processing capacity of the visual system. The selection of behaviorally relevant information from such cluttered scenes is mediated by visual attention. If one directs attention, for example, to a particular location in the visual field, information processing is greatly facilitated in the attended location and suppressed at nonattended locations (e.g., Treisman, 1969; Posner, 1980; Driver and Baylis, 1989). At the neural level, attending to a particular location or to a particular object feature is often accompanied by response enhancement in visual extrastriate cortex as demonstrated in functional imaging and event-related potential studies in the human (Corbetta et al., 1991; Heinze et al., 1994; Mangun, 1995; Beauchamp et al., 1997; Clark et al., 1997; O'Craven et al., 1997; Rees et al., 1997; Woldorff et al., 1997; Buechel et al., 1998; Kastner et al., 1998; Tootell et al., 1998; Wojciulik et al., 1998).

Single-cell recording studies in monkeys from areas in the ventral processing pathway, which is important for object recognition (Ungerleider and Mishkin, 1982), have shed light on the neural mechanisms underlying the attentional selection of a relevant object from a cluttered

scene. When multiple stimuli are presented simultaneously in a neuron's receptive field (RF) in areas V2, V4, or the inferior temporal cortex, and the animal directs its attention to one of them, the neuron's response is determined primarily by the attended stimulus (Moran and Desimone, 1985; Chelazzi et al., 1993, 1998; Reynolds et al., 1999). Recent work suggests that this attentional selection operates by biasing an underlying competitive interaction among multiple stimuli in the visual field. The most direct evidence for such competition is the fact that the response to an otherwise effective stimulus presented within a neuron's RF is reduced when a second stimulus is presented simultaneously at a different location within the same RF (Sato, 1989; Miller et al., 1993; Reynolds et al., 1999). Attending to the effective stimulus eliminates the suppressive influence of the second stimulus (Moran and Desimone, 1985; Reynolds et al., 1999). Thus, spatially directed attention operates by counteracting the suppressive influences of nearby stimuli, thereby enhancing information processing at the attended location. Additional evidence for the top-down bias favoring an attended stimulus location is the finding that stimulus-evoked responses to a RF stimulus are sometimes higher in areas V2 and V4 when the stimulus is attended (Spitzer et al., 1988; Motter, 1993), and, strikingly, the spontaneous (baseline) firing rates are 30%–40% higher in these same areas when the animal is cued to attend to a particular stimulus location within the RF even when no stimulus is present there, i.e., in the absence of visual stimulation (Luck et al., 1997). Taken together, these findings have suggested a "biased competition" account of attention, according to which attention directed to a location biases activity in visual cortex in favor of any stimulus presented at that location. When multiple stimuli appear in the visual field, the cells representing the stimulus at the attended location "win," thereby suppressing cells representing distracting stimuli at nearby locations (Desimone and Duncan, 1995; Duncan, 1996; Desimone, 1998).

In recent functional magnetic resonance imaging (fMRI) studies, we found evidence for similar mechanisms in human extrastriate cortex (Kastner et al., 1998). Multiple stimuli in the visual field were shown to interact in a mutually suppressive way when presented simultaneously but not when presented separately. Spatially directed attention to one stimulus location reduced these interactions by partially cancelling out their suppressive effects, as demonstrated by greater effects of attention on stimuli presented simultaneously than on those presented separately. These results suggest that modulation of sensory suppression by directed attention may provide a key mechanism of attentional selection in human extrastriate cortex. In the present study, we asked if top-down biasing signals could be found in human visual cortex *in the absence of visual stimulation*, similar to the increases in baseline firing rates demonstrated in monkey extrastriate cortex, and, if so, from which areas these top-down feedback signals might derive.

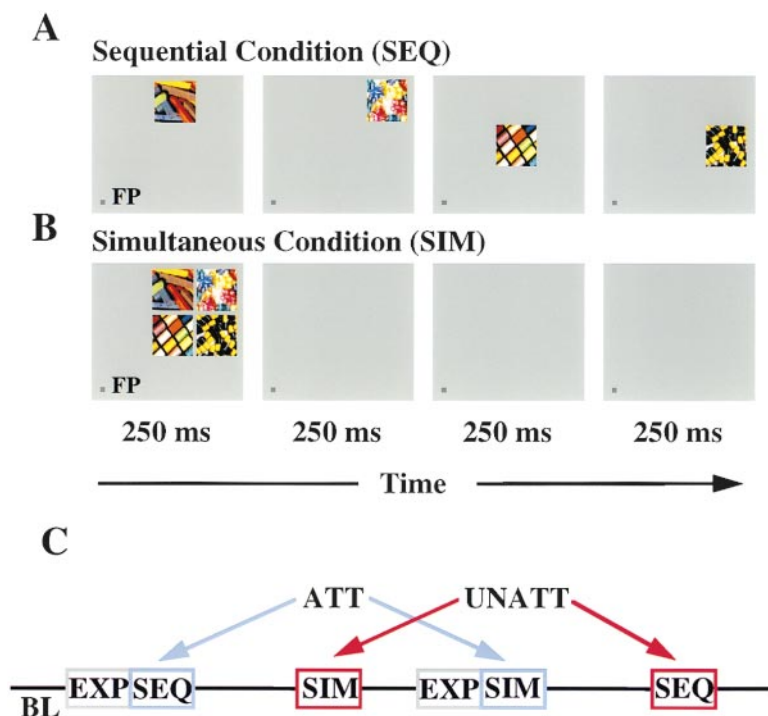‡ To whom correspondence should be addressed (e-mail: sabine@ln.nimh.nih.gov).

A
Sequential Condition (SEQ)

. FP

B
Simultaneous Condition (SIM)

. FP

250 ms   250 ms   250 ms   250 ms

Time ⟶

C

ATT   UNATT

BL EXP SEQ ———— SIM — EXP SIM ———— SEQ

Figure 1. Experimental Design

Four complex images were presented in four nearby locations at 6°–10° eccentricity from a fixation point (FP) either sequentially (A) or simultaneously (B). Presentation time was 250 ms, followed by a blank period of 750 ms, on average, in each location. A stimulation period of 1 s is shown, which was repeated in blocks of 10 s interleaved with blank periods (BL, shown in [C]). Two attentional conditions were tested (C): an unattended (UNATT), during which subjects maintained fixation, and an attended (ATT), during which subjects covertly directed attention to the location closest to fixation and counted the occurrences of one of the images. An attended condition was indicated 10 s before the onset of visual presentations. During this period (EXP), subjects covertly directed attention to the target location expecting the occurrences of the presentations. Blocks with expectation and attended presentations could be either the first and third, as shown in (C), or the second and fourth with the sequence counterbalanced across scans.

Results

Five subjects were tested in a modified version of a previously used block design (Kastner et al., 1998), in which epochs of visual presentations alternated with blank presentations as the subjects maintained fixation at a central fixation point (Figure 1C). During visual presentations, four complex colorful images were presented in four nearby locations to the periphery of the upper right quadrant either sequentially or simultaneously (Figures 1A and 1B). The physical stimulation parameters in each of the four locations were identical. However, sensory suppressive interactions among stimuli could take place only in the simultaneous and not in the sequential condition. In addition to the different visual presentation conditions, two attentional conditions were tested: an unattended condition (UNATT, Figure 1C), during which subjects maintained fixation and ignored the peripheral visual stimuli, and an attended condition (ATT, Figure 1C), during which subjects covertly directed attention to the location closest to fixation and counted the occurrences of one of the images, which was indicated before the scan started. The attended presentations were indicated by a marker next to the fixation point, which was presented briefly 11 s before the onset of the visual presentations. The subjects' task was to covertly direct attention to the target location as soon as the marker was shown and to expect the occurrence of the stimulus presentations (expectation period [EXP], Figure 1C). In this way, the effects of attention in the presence (ATT) and absence (EXP) of visual stimulation could be studied.

Visual Cortex

The complex images evoked significant activity in the unattended condition in visual areas V1, V2, VP, V4, and TEO of the left hemisphere in all subjects. As the border between V2 and VP could not be distinguished unequivocally in some of the subjects, the combined region will henceforth be referred to as V2. The locations of the activations were in the ventral parts of these areas, consistent with the locations of stimuli in the upper right visual field. This is illustrated for a single subject in Figure 2A. The same areas were activated in the attended condition, but activated volumes averaged across subjects were significantly greater in V4 (38% ± 12% [mean ± SEM]) and TEO (81% ± 12%) (ANOVA: main attentional effect, $p < 0.05$; cortical area and attentional effect, $p < 0.05$); there was no increase in volume due to attention in V1 or V2. During the 10 s expectation period that preceded the attended presentations, the same parts of areas V2, V4, and TEO were significantly activated in all subjects and of area V1 in two of five subjects (see Table 1). This activity was related to directing attention to the target location in the absence of visual stimulation and is shown for a single subject in Figure 2B. It should be noted that the increase in activity during expectation was retinotopically specific inasmuch as it was only seen in areas with a spatial representation of the attended location in the upper right quadrant. As shown in Figure 2B, the ventral portion of the lingual gyrus and medial parts of the fusiform gyrus of the left hemisphere, which contain the upper right visual field representations of V2 and V4, were activated.

An analysis of the time series of the fMRI signal (Figure 3) and the mean signal changes (Figure 4A) averaged across subjects showed that signals increased in all ventral visual areas during the expectation period (gray shaded epochs in Figure 3; EXP_{SF}, Figure 4A) with the strongest effect in V4 (repeated measures ANOVA: main effect of area, $p < 0.01$). This increase of activity, which we will term the baseline increase, was followed by a

A
Unattended Presentations versus Control

V1　V2　VP　V4　TEO

B
Expectation versus Control
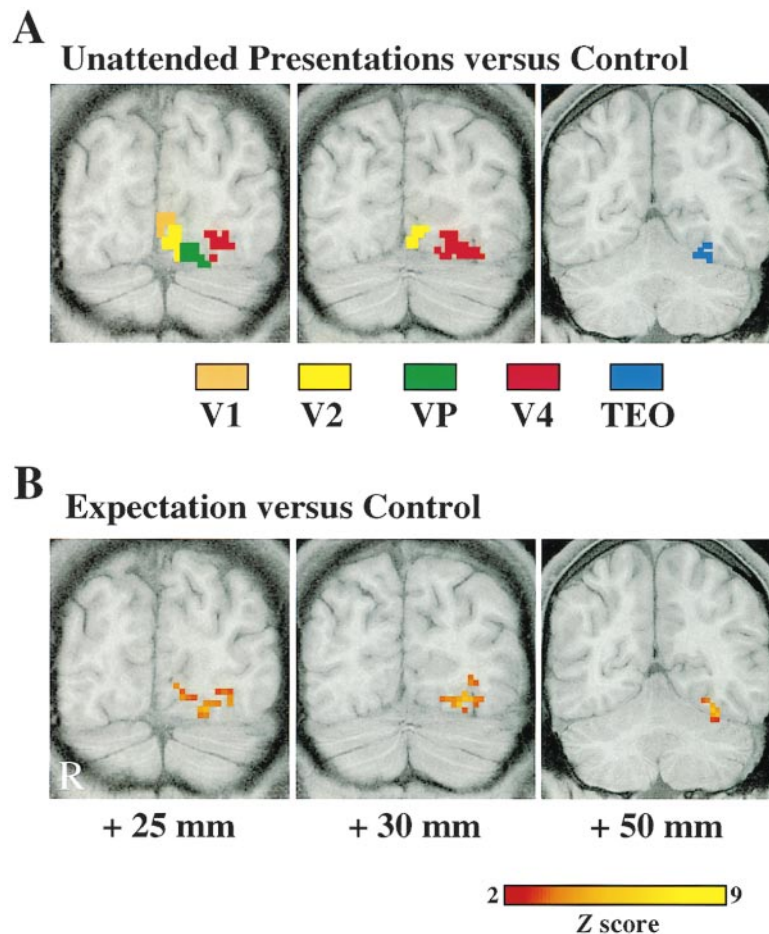

+ 25 mm　　+ 30 mm　　+ 50 mm

2 ▮▮▮▮ 9
Z score

Figure 2. Activated Areas in Visual Cortex

(A) Areas in ventral visual cortex activated by the complex images in the unattended condition compared to the subsequent blank presentations (control) plotted onto coronal slices of a single subject at different distances from the posterior pole. Activated voxels were assigned to areas V1, V2, VP, V4, and TEO as determined by retinotopical mapping. (B) Activated voxels in the same subject and the same slices contrasting the expectation period with the respective blank period preceding an unattended presentation (control). Areas V2, V4, and TEO showed significant clusters of activation. R, right hemisphere.

further increase of activity after the onset of the visual presentations (blue shaded epochs in Figure 3). In all areas, the signals evoked by visual presentations were larger than the baseline increase (Figures 3 and 4A; ATT versus EXP, $p < 0.01$ in V1, V4, TEO and $p < 0.05$ in V2). During alternating expectation periods, a small ($0.2° \times 0.2°$) black dot was presented as a spatial cue in the target location in order to reduce the subjects' working memory load of the attended location. No differences in the magnitude of baseline increases were seen in conditions with or without this cue, suggesting that the baseline increases do not depend to a significant degree on spatial working memory.

Because the baseline increase was obtained by comparing conditions during which subjects directed attention to a peripheral target location with conditions during which subjects simply maintained fixation without being engaged in an attentional task, it could be argued that the baseline increase was due to nonspecific effects, such as arousal. Although the retinotopic specificity of the baseline effects argued against this possibility, we ran an additional control experiment to rule it out. In this control, the activity in the peripheral attention task was compared with the activity in a task that engaged the subjects' attention at fixation. In this fixation task, subjects counted Ts or Ls presented at a rapid rate, a task shown to be of high attentional load (cf. Kastner et al.,

1998). We measured the activity in the peripheral field representation of the upper quadrant when subjects covertly attended to that location compared to the activity when subjects attended to the fixation location. The baseline effect in this control condition was nearly identical to what we had found in the main experiment ($EXP_{T/L}$, Figure 4A), demonstrating that the baseline increase was due to spatially directing attention to the peripheral location.

In many respects, the activity evoked by unattended and attended stimulus presentations in the current paradigm confirmed our earlier findings (Kastner et al., 1998). As found before, simultaneously presented stimuli evoked weaker responses than sequentially presented stimuli in V2 ($p < 0.05$), V4 ($p < 0.001$), and TEO ($p < 0.05$) but not in V1 (Figures 3 and 4A) during the unattended visual presentations. This sensory suppression effect increased from V1 to V4 (interaction of cortical area and presentation condition, $p < 0.05$). In TEO, sensory suppression was not different from that seen in V2.

Also, as found before, activity to both sequentially and simultaneously presented stimuli increased significantly during the attended visual presentations in V2 ($p < 0.01$), V4 ($p < 0.0001$), and TEO ($p < 0.01$) but not in V1 (Figures 3 and 4A). However, simultaneously presented stimuli evoked stronger attentional response enhancement than sequentially presented stimuli in these areas (V2,

Table 1. Talairach Coordinates of Activated Areas in Visual, Parietal, and Frontal Cortex

Area	Brodmann Area (BA)		X	Y	Z	Z score	N
Visual Cortex							
Unattended versus Blank							
V1	17	L	−6 (6)	−85 (5)	+11 (6)	5.5 (1.4)	5
V2/VP	18	L	−13 (6)	−80 (4)	−12 (6)	7.4 (2.8)	5
V4	19	L	−22 (5)	−79 (3)	−18 (3)	9.3 (2.1)	5
TEO	19/37	L	−30 (6)	−61 (5)	−11 (7)	6.7 (1.8)	5
Expectation versus Control							
V1	17	L	−5 (4)	−86 (4)	+8 (10)	3.1 (0.5)	2
V2/VP	18	L	−13 (8)	−82 (6)	−19 (5)	6.2 (2.2)	5
V4	19	L	−29 (8)	−79 (8)	−25 (3)	6.8 (3.1)	5
TEO	19/37	L	−30 (5)	−65 (5)	−21 (6)	4.4 (0.8)	5
Parietal Cortex							
Expectation versus Control							
IPS	7	L	−27 (4)	−78 (7)	+38 (14)	7.7 (0.8)	5
SPL	7	L	−18 (3)	−63 (6)	+54 (2)	6.5 (1.1)	5
	7	R	+16 (7)	−61 (7)	+57 (8)	8.3 (1.3)	5
IPL	40	L	−37 (1)	−32 (8)	+59 (1)	5.2 (2.1)	3
	40	R	+38 (3)	−34 (6)	+57 (3)	5.8 (1.9)	3
Frontal Cortex							
Expectation versus Control							
FEF	6	L	−41 (7)	+1 (6)	+49 (5)	7.9 (1.8)	4
	6	R	+35 (6)	−9 (6)	+55 (10)	7.7 (1.3)	4
SEF	6		−1 (4)	−1 (5)	+61 (13)	6.2 (0.9)	4
MFG	9	L	−30 (4)	+33 (4)	+30 (15)	5.6 (0.8)	3
	9	R	+32 (1)	+32 (9)	+39 (5)	5.9 (3.1)	4

Values are means (±SD) of peak coordinates in millimeters. L, left; R, right; N, number of subjects showing significant clusters of activation.

0.57% compared to 0.32%; V4, 0.92% compared to 0.59%; TEO, 0.66% compared to 0.52%), partially counteracting the sensory suppression effect. The interaction between the sensory suppression effect and the attentional effect was significant in V4 ($p < 0.05$).

In order to study the relation between attentional effects on visually evoked activity and the baseline increase evoked by directing attention to the target location in the absence of visual stimulation, two measures were defined: an attentional modulation index (AMI) and a baseline shift index (BSI). The AMI estimates the attentional enhancement of visually evoked activity, i.e., the increase in response to the attended compared to the unattended stimulus presentations. The AMI was calculated separately for the responses to sequential (AMI_{SEQ}) and simultaneous (AMI_{SIM}) presentations (Figure 4B). The BSI estimates the increase in baseline activity during expectation; BSIs preceding simultaneous or sequential presentations were not different and were therefore averaged (EXP in Figure 4B). The AMI and BSI typically ranged from +1 to −1, with positive values indicating response enhancement and negative values indicating response suppression. Because the AMI and the BSI were normalized to the same values, these measures allow for a direct comparison of the magnitude of the attentional effects on the baseline activity and on the visually evoked responses. In V2 and V4, the BSIs were similar in magnitude to the $AMIs_{SIM}$ but were significantly larger than the $AMIs_{SEQ}$ ($p < 0.01$) (Figure 4B). In V1, the BSI was significantly larger than both AMIs ($p < 0.01$); in TEO, the BSI was not different from either AMI (Figure 4B).

In summary, directing attention to a peripheral target location and expecting the occurrences of visual stimuli in that location led to an increase of baseline activity in striate and extrastriate cortex. The magnitude of the baseline increase was similar to the magnitude of attentional effects on responses to simultaneously presented visual stimuli, but was larger than the magnitude of attentional effects on responses to stimuli presented separately.

Frontal and Parietal Cortex

Areas in frontal and parietal cortex activated during the expectation period are depicted for a single subject in Figure 5. Across all subjects, areas in the frontal eye field (FEF), the supplementary eye field (SEF), the superior parietal lobule (SPL), and the intraparietal sulcus (IPS) were found to be activated in this condition (Figure 5A and Table 1). In addition, but less consistently, areas in the inferior parietal lobule (IPL) and the middle frontal gyrus (MFG) were found to be activated (Table 1). Areas in the FEF, SPL, and IPL were activated bilaterally without hemispheric differences. Lateralized hemispheric activations were seen in IPS and MFG, but they were inconsistent across subjects.

The time series of the fMRI signal, the mean signal changes, and the AMI and BSI averaged across subjects are shown in Figures 6 and 7 for IPS, SPL, FEF, and SEF. In SPL, FEF, and SEF, there was a similar increase in the fMRI signals during expectation ($p = 0.13$), and this increase was greater than that seen in visual cortex ($p < 0.05$) (gray shaded epochs in Figures 6 and 7A). In
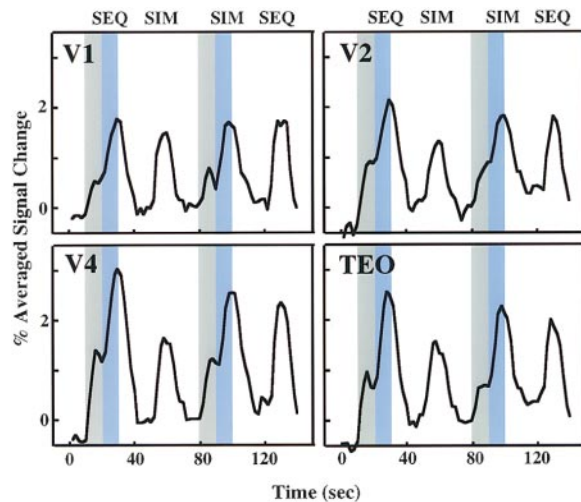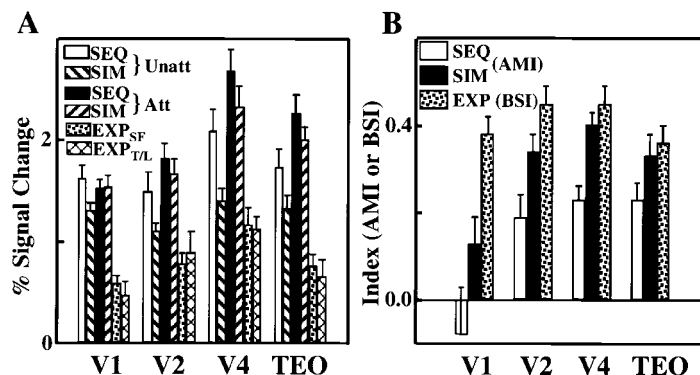
Figure 3. Time Series of fMRI Signals in Visual Cortex

Time series of fMRI signals in V1, V2, V4, and TEO averaged over all subjects. Gray shades indicate the expectation period, blue shades the attended presentations. Blocks with unattended presentations are shown without shading. During the unattended presentations, sequentially presented stimuli evoked stronger activity than simultaneously presented stimuli. This sensory suppression effect was strongest in V4 and TEO. In the attended condition, signals to simultaneously presented stimuli increased to a larger extent than to sequentially presented stimuli. When subjects directed attention to the target location during the expectation period, activity increased in the absence of visual presentations and further increased after the onset of visual stimuli. This baseline increase was seen in all visual areas under investigation, with the strongest effect in V4. SEQ, sequentially presented stimuli; SIM, simultaneously presented stimuli.

sustained activity throughout the expectation period and the attended stimulus presentations (blue shaded epochs in Figures 6 and 7A). In IPS, the increase in baseline activity with attention was followed by a strong increase in the response to the visual stimuli with attention ($p < 0.001$) (blue shaded epochs in Figures 6 and 7A). In this respect, the response pattern of the IPS resembled that of ventral extrastriate areas.

In all frontal and parietal areas, there was a significant effect of attention on activity evoked by visual stimuli (ATT versus UNATT; FEF, SPL, and IPS, $p < 0.001$; SEF, $p < 0.01$; Figures 6 and 7). The magnitude of attentional response modulation was similar in FEF, SEF, and SPL but less strong both in IPS ($p < 0.001$) (Figure 7B) and in ventral extrastriate cortex ($p < 0.0001$). This reflects the fact that minimal activity was evoked during the unattended condition in FEF, SEF, and SPL. Sequentially and simultaneously presented stimuli did not evoke significant differences in activity in any frontal or parietal area, suggesting that visual stimuli were not competitively interacting in these regions (Figures 6 and 7A). Accordingly, the attentional effects on sequentially and simultaneously presented stimuli were similar in these areas (Figure 7B). In all parietal and frontal areas, baseline increases were significantly stronger than attentional effects on visually evoked activity (BSI versus AMI, $p < 0.05$; Figure 7B).

In summary, the effect of attention in SPL, FEF, and SEF was a sustained and relatively constant amount of enhanced activity during the periods of both expectation and attended visual presentations. The increases in both baseline activity and the attentional effects on visually evoked activity were larger than in visual cortex. This is summarized in Figure 8, in which AMIs averaged across presentation conditions and BSIs are plotted for each area. By contrast, the activity in IPS resembled, in many respects, that seen in ventral extrastriate areas. However, unlike in ventral extrastriate cortex, sequentially and simultaneously presented stimuli did not evoke response differences in the IPS, suggesting that suppressive sensory interactions among stimuli were absent or very small in this area.

IPS, this baseline increase was less strong than in the other parietal and frontal areas ($p < 0.01$) and did not differ from that found in visual areas V1, V2, and TEO (gray shaded epochs in Figures 6 and 7A) ($p = 0.41$). In SPL, FEF, and SEF, the increase in baseline activity during expectation was not followed by a further increase of activity evoked by the onset of visual stimulation (ATT versus EXP, $p = 0.30$), thereby resulting in

Figure 4. Mean Signal Changes and Indices of Attentional Modulation and Baseline Shift in Visual Cortex

(A) Mean signal changes in V1, V2, V4, and TEO, averaged across subjects. For each subject, the five peak intensities of the fMRI signal obtained during attended and unattended presentations and during the expectation period were averaged. Activity during the expectation period (EXP) is shown compared to two different control conditions: in the first, used in the main experimental design, subjects simply maintained fixation (EXP_{SF}; SF, simple fixation); in the second, used in the control experiment, subjects counted Ts or Ls at fixation ($EXP_{T/L}$).

(B) Attentional response modulation on sequentially and simultaneously presented stimuli as quantified with an AMI, which normalizes the attentional effects to the activity evoked in the respective attended condition. Similarly, the BSI indicates the amount of baseline increase relative to the activity evoked by the subsequent attended presentations. BSIs are only shown for data obtained with the main experimental design. In V2, V4, and TEO, the baseline increases were similar to the attentional effects on simultaneous presentations but stronger than the attentional effects on sequential presentations. Vertical bars indicate SEM.
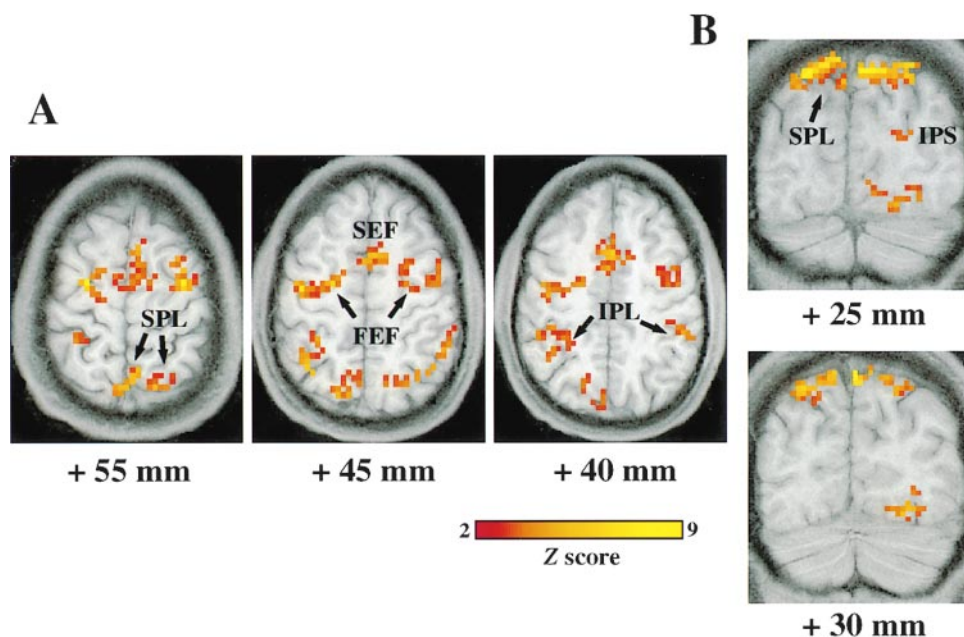
Figure 5. Areas in Frontal and Parietal Cortex Activated during Expectation

Same subject as in Figure 2.

(A) Activated areas in frontal (SEF, FEF) and parietal (SPL, IPL) cortex obtained in session 2 and depicted on axial slices. The approximate Talairach plane is indicated for each slice.

(B) Activated areas in parietal cortex (SPL, IPS) obtained in session 1. Same coronal slices as shown in Figure 2. The distances from the posterior pole are indicated.

Discussion

Biasing Signals in Visual Cortex

In this study, we demonstrate increases of activity in human visual cortex *in the absence of visual stimulation* caused by covertly directing attention to a particular location and expecting the occurrence of visual stimuli at that location. The attentional effects on the baseline activity in striate and extrastriate areas were in the range of 0.5%–1.1% mean signal change or 35%–50% of the response to visual stimuli. The increases in baseline activity appear to be qualitatively similar to the increases in maintained (spontaneous) firing rate with attention, as demonstrated in single-cell recording studies in monkey extrastriate cortex by Luck and colleagues (1997). In these studies, the monkey was cued to attend to a location within or outside a neuron's RF in the absence of visual stimulation. When the monkey attended within the RF, the maintained firing rate increased by 43% in V2 and by 30% in V4 relative to the maintained firing rate seen when the monkey attended outside the RF. Though it is difficult to compare the magnitude of the effects found with the different techniques, it is likely that a similar modulation of maintained firing rate was the basis for the signal changes measured with fMRI. The most notable difference between the present study and the single-cell recording study is that we found a significant baseline increase in V1, which was not found by Luck et al. However, the baseline increase we obtained in V1 was clearly seen only in the averaged signals across all subjects and in two of five individual subjects. Hence, the effects in V1 may be more variable or sometimes too small to be measured in individual subjects.

The baseline increase evoked by directing attention to a target location in anticipation of a behaviorally relevant stimulus at that attended location has been interpreted, in the framework of the biased competition account of
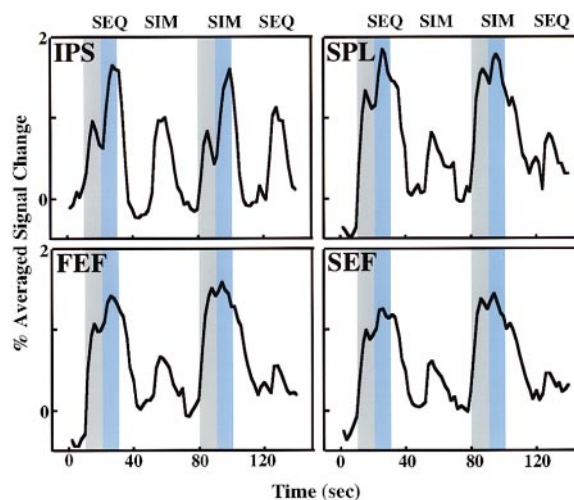

Figure 6. Time Series of fMRI Signals in Frontal and Parietal Cortex

Time series of fMRI signals in IPS, SPL, FEF, and SEF averaged across subjects. Conventions as in Figure 3. During the expectation period, signals increased to a greater degree in FEF, SEF, and SPL than in visual cortex; this response increase was not followed by a further increase after the onset of the stimuli resulting in a sustained activity. The pattern of activity in IPS resembled more that in extrastriate areas than in SPL, FEF, and SEF. None of the frontal or parietal areas showed sensory suppressive effects among interacting visual stimuli.
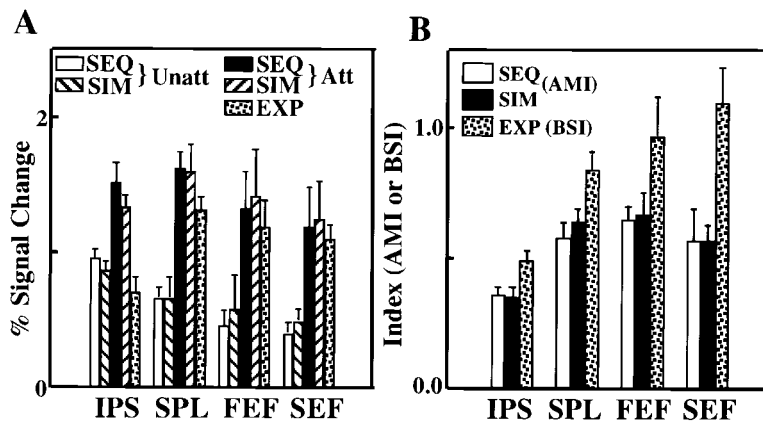
A

B

Figure 7. Mean Signal Changes and Indices of Attentional Modulation and Baseline Shift in Frontal and Parietal Cortex

All conventions as in Figure 4. All areas showed significant attentional response enhancement. Attentional modulation on sequentially and simultaneously presented stimuli was similar in all areas. Baseline increases were stronger than attentional modulation effects in all areas.

attention (Desimone and Duncan, 1995), to reflect a top-down feedback bias in favor of the attended location (Luck et al., 1997; Desimone, 1998). In agreement with this interpretation, the baseline increase was observed in all visual areas that contained a representation of the attended portion of the visual field. Thus, in addition to V1 and ventral stream areas V2, V4, and TEO, activity during the expectation period was also observed in dorsal stream areas V3A and MT (to be reported in detail elsewhere). These data thus support the notion that the increase in baseline activity is spatially dependent and retinotopically organized, just like the attentional enhancement effects on visual stimuli (Woldorff et al., 1997; Kastner et al., 1998; Tootell et al., 1998). However, we cannot rule out the possibility that the baseline increase is object-based rather than spatially based inasmuch as the increases were found in the same areas that were activated by the complex images. Even though these areas include MT and V3A, they too may be involved in the processing of particular object features contained in the images.

It may be argued that the baseline increases during expectation reflect the memory of the attended stimulus location rather than a top-down feedback bias in favor of the attended location. We have addressed this possibility by presenting a spatial cue in that location instead of a blank screen, thereby reducing the subjects' spatial working memory load. No differences in baseline increases were found in conditions with and without a cue, suggesting that the baseline increases did not depend heavily on spatial working memory. In general, however, there is a close relationship between the neural mechanisms for attention and working memory, and these mechanisms may be difficult to disentangle (Desimone and Duncan, 1995).

Another possibility is that the baseline increases reflected the activated memory of particular target features. Luck et al. (1997) investigated this possibility by comparing the baseline activity in trials in which preferred stimuli were used as targets for the V4 cells to trials in which nonpreferred stimuli were used as targets. They found no difference in baseline activity between these two conditions. Therefore, it seems unlikely that the baseline effect depends on the activated memory of features of the target stimulus. Further investigations, however, are needed to clarify how the expectation of

different object features may influence the baseline effect in the multiple areas of human visual cortex.

Because the baseline increase was obtained by comparing a condition during which subjects covertly directed attention to a peripheral target location with a condition during which subjects simply maintained fixation, it may be argued that the baseline increase was due to nonspecific effects, such as arousal, or any other general difference between these two conditions. Our findings speak clearly against this notion. First, we found the same baseline increase in a control experiment, in which we compared the peripheral attention task to a condition during which subjects performed a high attentional load task at fixation. Second, baseline increases in areas V1, V2, and V4 were found only in the portion of the visual field representations that contained the attended location; i.e., the effects had retinotopic specificity (see Figure 2A). Nonspecific effects of attention, such as arousal, would have influenced all parts of the visual field representations.
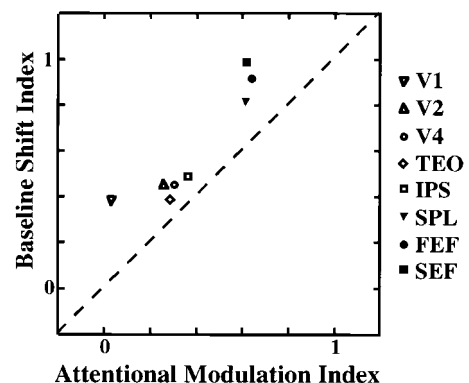

Figure 8. The Relation of Attentional Modulation and Increases in Baseline Activity in Frontal, Parietal, and Visual Cortex

For each area, the BSI is plotted against the mean AMI, averaged across sequential and simultaneous conditions. Attentional modulation and baseline increases were similar in ventral extrastriate areas V2, V4, and TEO and parietal area IPS. In V1, a relatively strong increase of baseline activity was seen, whereas attentional modulation was weak. SPL, FEF, and SEF showed a similar relation of attentional modulation and baseline increases. Both effects were, however, stronger than in extrastriate cortex and IPS.

Candidate Areas Generating Biasing Signals

We interpret the increase in baseline activity in visual cortex to reflect a top-down feedback bias from areas outside visual cortex. From what source might these signals arise? The likeliest candidates are SPL, FEF, and SEF. All three of these areas were found to have stronger baseline increases than ventral stream areas and the IPS. Further, such increases were not followed by additional activity evoked by the onset of visual stimuli. This sustained activity during the expectation period and the attended presentations thus reflected the attentional demands of the task more than sensory processing. The anatomical connections of SPL, FEF, and SEF put them in a position to serve as sources of top-down biasing signals. In the monkey, FEF and SEF are reciprocally connected with ventral stream areas (Ungerleider et al., 1989; Webster et al., 1994) and posterior parietal cortex (Cavada and Goldman-Rakic, 1989). The posterior parietal cortex is connected with ventral stream areas via the lateral intraparietal area (LIP) (Webster et al., 1994).

Based on lesion data, both Mesulam (1981) and Posner and Petersen (1990) have proposed a distributed attention network consisting of areas in posterior parietal cortex, the frontal eye field, cingulate cortex, and structures of the reticular formation. Functional imaging studies support this idea inasmuch as the SEF, FEF, and SPL have been shown to be activated in a variety of tasks requiring covert shifts of attention to peripheral spatial locations (Corbetta et al., 1993, 1998; Nobre et al., 1997; Vandenberghe et al., 1997; Kastner et al., 1998, Soc. Neurosci., abstract). The attention-related activity in these areas has been interpreted as an enhancement of the response to visual stimuli. This interpretation is in agreement with single-cell recording studies, which have shown response enhancement in regions of parietal cortex during covert shifts of attention to peripheral visual stimuli (Robinson et al., 1978; Bushnell et al., 1981; Colby et al., 1996). In the FEF and SEF, such response enhancement was originally shown only in the context of activity related to the preparation of saccadic eye movements (Wurtz and Mohler, 1976; Goldberg and Bushnell, 1981). Recent recording studies suggest, however, that the response enhancement in these frontal areas during covert shifts of attention to peripheral visual stimuli does not depend on the subsequent execution of saccades (Bon and Lucchetti, 1997; Kodaka et al., 1997). In all of these studies, the effects of attention on baseline activity could not be separated from the effects of attention on visual responses, because the activity was recorded in the presence of visual stimuli. Because we found a similar magnitude of activity during directed attention in the absence and in the presence of visual stimulation in areas SPL, FEF, and SEF, our results suggest that the response enhancement in these areas was largely due to the attentional operations themselves and not to attentional modulation of visual responses. It would be interesting to investigate the responses of single units during expectation and attended stimulus presentations in parietal and frontal cortex to further clarify the physiological basis of the attentional response enhancement seen in these areas.

Attentional Response Modulation in Visual Cortex

In confirmation of our previous studies (Kastner et al., 1998), we found that multiple stimuli in the visual field interacted in a mutually suppressive way in areas of the ventral stream and that directed attention led to a stronger enhancement of responses to multiple simultaneously presented stimuli than to multiple stimuli presented separately. This is in agreement with a number of single-cell recording studies, which have shown greater effects of attention evoked by stimuli presented together than when the same stimuli were presented alone, especially when the stimuli were shown within the neuron's RF (Moran and Desimone, 1985; Chelazzi et al., 1993, 1998; Treue and Maunsell, 1996; Luck et al., 1997; Reynolds et al., 1999). Taken together, the imaging and physiology results suggest that multiple stimuli in the visual field compete for neural representation. One way to bias the competition in favor of one of the stimuli is by directing attention to it (Desimone and Duncan, 1995; Desimone, 1998). This may be an important mechanism for the selection of relevant and the filtering of irrelevant information in the visual system.

Response enhancement due to attention in human ventral extrastriate cortex has been shown in several previous imaging studies (Corbetta et al., 1991; Heinze et al., 1994; Clark et al., 1997; Rees et al., 1997; Wojciulik et al., 1998). However, in light of our current findings, it is not clear whether such enhancement was due to an increase in baseline activity, to an increased response evoked by the visual stimuli, or to both. Data from the present study speak against the notion that attentional response enhancement simply reflected a baseline increase in activity. First, we found a significant increase in baseline activity with attention in V1 without a concomitant increase in the visually evoked response with attention. Second, the effects of attention on the baseline activity were larger than the effects of attention on visually evoked activity to sequentially presented stimuli in V2 and V4.

The fact that increases in baseline activity and the attentional effects on visually evoked activity are not tightly coupled suggests that the two effects derive from different but partially overlapping populations of neurons. The increases in baseline activity might be due, for example, to an activation of large populations of neurons containing the attended spatial location within their receptive fields and responding relatively nonspecifically to the various features of the expected stimuli, whereas the attentional effects on visually evoked activity might be subserved by a smaller population of neurons that not only contain the attended location within their receptive fields, but also respond selectively to particular stimulus features contained in the complex images.

A Visual Area in the Intraparietal Sulcus

We have identified an area in the depth of the IPS, just anterior to V3A, that responded in many respects like ventral stream extrastriate areas. In IPS, baseline increases during expectation were followed by large additional increases in activity after the onset of visual stimuli. This response pattern was very different from that seen in SPL, which showed sustained activity through expectation and subsequent presentation of visual stimuli. We interpret the pattern of responses in IPS to indicate that the area was strongly driven by visual stimuli. This visually evoked activity could be modified by top-down influences such as attention. However, the responses evoked in IPS to visual stimuli were smaller

than those seen in V2, V4, and TEO. Further, IPS did not show sensory suppressive interactions among stimuli (i.e., a stronger response to sequentially than to simultaneously presented stimuli) and, accordingly, did not show the attentional effects seen in ventral stream extrastriate areas (i.e., stronger attentional effects on simultaneously than on sequentially presented stimuli). In these respects, the response pattern in IPS resembled more those seen in SPL, SEF, and FEF. Therefore, it might be concluded that the IPS operates at an intermediate level in the hierarchy of visual processing between lower-tier areas, such as V4 and TEO, and higher-tier parietal and frontal areas.

It is unknown which area in the macaque cortex may be homologous to IPS. One possibility is area LIP, which is located in the lateral intraparietal sulcus and has corticocortical connections with many extrastriate areas, including V3A, MT, V4, and TEO, as well as with higher-order areas, such as area 7a on the inferior parietal lobule and the FEF (Blatt et al., 1990; Webster et al., 1994). In agreement with our findings in IPS, LIP neurons respond to stationary visual stimuli and show response enhancement when the monkey covertly directs attention to a stimulus (Colby et al., 1996). Interestingly, the maintained firing rate of LIP neurons increases during the period when the monkey expects a behaviorally relevant stimulus to appear (Bracewell et al., 1996; Colby et al., 1996); i.e., LIP neurons show a baseline shift similar to that seen in monkey V2 and V4 (Luck et al., 1997). Recent studies have shown that many LIP neurons show shape selectivity, and this selectivity is maintained during the delay period of a delayed match-to-sample task (Sereno and Maunsell, 1998). These response properties may explain why the IPS was driven by stimuli containing many different object features, as used in the present study. However, further investigations are needed to establish a homology between monkey LIP and human IPS, especially investigations demonstrating saccade-related activity in IPS, which is a characteristic property of many LIP neurons (Barash et al., 1991).

Experimental Procedures

Subjects
Five subjects (three females, ages 22–34) participated in the study, which was approved by the NIMH Institutional Review Board. All subjects were in good health with no past history of psychiatric or neurological diseases and gave their informed written consent. Subjects had normal or corrected-to-normal (with contact lenses) visual acuity.

Visual Task
Colorful, complex images were used as visual stimuli in a similar design as used previously (Kastner et al., 1998). Examples of stimuli out of a library of about 100 are given in Figures 1A and 1B. Four of these images, each $2° \times 2°$ in size, were presented in four nearby locations to the upper right quadrant at $6°–10°$ eccentricity from a fixation point. Stimuli were shown in two conditions: a sequential (SEQ) and a simultaneous (SIM). In the sequential condition, stimuli were presented alone in one of the four locations for 250 ms (Figure 1A). In the simultaneous condition, the four stimuli appeared together for 250 ms (Figure 1B). The order of stimuli and locations was randomized. The physical stimulation parameters in each of the four locations were identical in the two conditions, but sensory interactions among stimuli could take place only in the simultaneous and not in the sequential condition. During a given scan, sequential

and simultaneous conditions were presented in blocks of 10 s interleaved with blank periods in the sequence SEQ–SIM–SIM–SEQ (Figure 1C). Each scan started with a blank period of 20 s and ended with a blank period of 10 s. Different stimuli were used for different scans.

In addition to the two presentation conditions, an unattended and an attended condition were tested in the same scan. In the unattended condition (UNATT, Figure 1C), subjects were instructed to maintain fixation at a central fixation point and to ignore the peripherally presented stimuli. In the attended condition (ATT, Figure 1C), they covertly shifted attention to the stimulus location closest to fixation and counted the occurrences of one of the stimuli, which was indicated before the scan started. The blocks with directed attention to the display were cued by a marker, an oriented line ($1.5° \times 0.1°$) pointing to the target location, which was presented close to the fixation point. This marker appeared for a brief time (500 ms) 11 s before the attended presentations started. During this period, subjects directed attention to the target location expecting stimuli to occur (EXP, Figure 1C). This way, the effects of attention in the absence and in the presence of visual stimulation could be tested. During every other expectation period, a small ($0.2° \times 0.2°$) black dot was presented as a spatial cue at the target location 500 ms after the offset of the marker in order to reduce the subjects' spatial working memory load to the attended location; during the other expectation periods, the screen was blank. Blocks with expectation and attended presentations could be either the first and third, as shown in Figure 1C, or the second and fourth with the sequence counterbalanced across scans. After each scan, subjects reported the number of presentations of the image that they had counted at the target location in each attended block. In a control experiment, the same conditions were run while subjects performed a high attentional load task at fixation, which was to count Ts or Ls presented at a rapid rate during blank periods and unattended presentations (cf. Kastner et al., 1998). Before being scanned, subjects received three to four training sessions outside the scanner to learn to maintain fixation over several minutes; then they were trained in the attentional task for another three to four sessions. Each training session lasted 15–20 min. Eye movements were monitored during these training sessions.

Data Acquisition
Images were acquired with a 1.5 Tesla GE Signa scanner (Milwaukee, WI) using a standard head coil. Subjects were comfortably placed on their backs with their heads restrained and surrounded by soft foams in order to reduce head movements. Subjects were tested in two separate scanning sessions, each lasting for 2 hr. During each session, 10–12 scans were acquired. Functional images were taken with a gradient echo echoplanar imaging sequence (TR = 2 s, TE = 40 ms, flip angle = 90°). In session 1, ten contiguous coronal slices were taken, starting 15–20 mm from the posterior pole (thickness, 5 mm; in-plane resolution, 2.5 x 2.5 mm) and covering activation areas in occipital, posterior temporal, and parietal cortex. In session 2, ten contiguous axial slices were taken starting from the top of the brain (thickness, 5 mm; in-plane resolution, 3.125×3.125 mm) and covering activation areas in frontal and parietal cortex. All subjects were scanned in session 1; four of the five subjects were scanned in session 2.

Echoplanar images were compared with a coaligned high-resolution anatomical scan of the same subject's brain taken in the same session (3D SPGR, TR = 15 ms, TE = 7 ms, flip angle = 30°, 256×256 matrix, FOV = $160–200 \times 160–200$ mm, 28 coronal or axial slices [thickness, 5 mm]). Another high resolution anatomical scan of the whole brain was taken in a different session in order to perform spatial normalization in SPM (3D SPGR, TE = 5.4 ms, flip angle = 45°, 256×256 matrix, FOV = 240×240 mm, 124 sagittal slices [thickness, 1.5 mm]).

Visual stimuli were presented to the subjects as videotapes rear-projected onto a translucent screen placed 40 cm from the subject's feet with a magnetically shielded LCD projector. Stimuli could be viewed from inside the bore of the magnet via a mirror system attached to the head coil. Synchronization of the video presentation with the MR data acquisition was accomplished by manually starting the video the same time as the scanner.

Retinotopic Mapping

For each subject, retinotopic mapping was performed in a separate scanning session. Areas V1, V2, and VP were identified by determining the alternating representations of the vertical and horizontal meridians, which form the borders of these areas (see Kastner et al., 1998). This was accomplished by presenting high color– and luminance-contrast checker stimuli along the meridians flickering at 4 Hz. Since it was difficult to separate V2 and VP in some subjects, activity was averaged across the two areas in all subjects. Areas V4 and TEO were identified by their characteristic upper (UVF) and lower (LVF) visual field retinotopy. The UVF and the LVF are separated in V4 and located medially and laterally on the fusiform gyrus, whereas this separation is not seen in the region anterior to V4, which we term TEO (Kastner et al., 1998). UVF and LVF retinotopy was accomplished by presenting the complex images either to the upper right or the lower right quadrant.

Data Analysis

Between-scan head movements were corrected by aligning each image to a mean image of one of the scans obtained in the middle of the session using automatic image registration (AIR) software (Woods et al., 1993). Images were spatially smoothed in-plane with a small Gaussian filter (FWHM of 1.2 voxel lengths) and ratio-normalized to the same global mean intensity. Statistical analyses were restricted to brain voxels with adequate signal intensity (average intensity of >20% of the maximum value across voxels) and performed on both smoothed and unsmoothed data. The first five images of each scan were excluded from analysis. Statistical analyses were performed using multiple regression in the framework of the general linear model (Friston et al., 1995a, 1995b) with NIH fidap software. Square-wave functions matching the time course of the experimental design were defined as effects of interest in the multiple regression model. The square-wave functions contrasted (1) epochs with unattended visual presentations versus subsequent blank periods, (2) epochs with attended presentations versus subsequent blank periods, (3) epochs of attended versus unattended visual presentations, and (4) epochs of expectation with directed attention in the absence of visual stimulation, preceding the attended presentations, versus control epochs with blank presentations preceding the respective unattended visual presentations. The latter activity was defined as baseline, relative to which increases were measured. For each effect of interest, square-wave functions were convolved with a Gaussian model of the hemodynamic response (lag, 4.8 s; dispersion, 1.8 s) to generate idealized response functions, which were used as regressors in the multiple regression model. Additional regressors were included into the model to partially factor out variance due to baseline shifts between time series and linear drifts within time series. All statistical results have a single voxel Z threshold of 2.33 (degrees of freedom corrected for correlation between adjacent time points). Regions of interest (ROI) were located by identifying clusters of seven or more contiguous statistically significant voxels. Statistical significance ($p < 0.01$) of these clusters was assessed using random Gaussian field methods based on their spatial extent and peak height (Friston et al., 1994; Poline et al., 1997). Statistically significant clusters of voxels were overlaid on structural T1-weighted scans taken in the same session and in the same plane. Activity in visual cortex was assigned to retinotopically organized areas based on meridian mapping. FEF and SEF in frontal cortex were identified by their reported locations in the literature (e.g., Petit et al., 1997, 1998; Corbetta et al., 1998). All time course analyses reported in this paper were performed on unsmoothed data. Time series of fMRI intensities, presented as group data, were averaged over all voxels in a given ROI, normalized to the mean intensity obtained during the control condition and collapsed across the different sequences of unattended and attended presentations. Time series are presented in the sequence shown in Figure 1C. For each subject, the five peak intensities of the fMRI signal obtained during unattended and attended presentations and expectation periods, respectively, were averaged, resulting in mean signal changes. These values were further quantified by defining an AMI ($AMI_{SEQ} = [ATT_{SEQ} - UNATT_{SEQ}]/ATT_{SEQ}$ where ATT_{SEQ} and $UNATT_{SEQ}$ = averaged responses during either attended [ATT] or unattended [UNATT] sequential presentations; accordingly, an AMI_{SIM} was computed for responses to simultaneous presentations) and a BSI ($BSI_{SEQ} = 1 - [(ATT_{SEQ} - EXP_{SEQ})/ATT_{SEQ}]$ where EXP_{SEQ} and ATT_{SEQ} = averaged responses during either expectation of visual stimuli preceding sequential presentations [EXP] or attended [ATT] sequential presentations; accordingly, a BSI_{SIM} was computed for responses during the expectation and presentation of simultaneously presented stimuli). Statistical significance was assessed with repeated measures ANOVAs on the peak intensities of the fMRI signal. Two-way and three-way ANOVAs were calculated to assess significance for indices. For each subject, Z score maps and structural images were transformed into the standard stereotactic Talairach space (Talairach and Tournoux, 1988) using SPM96b. For this purpose, structural and functional partial volumes were aligned to a high-resolution structural whole brain volume from the same subject using AIR software in Medx.

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